

CLAIMS

What is claimed is:

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1. An isolated nucleic acid comprising a nucleotide sequence encoding a Tcl-1b protein, wherein said nucleotide sequence is a cDNA sequence.

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2. The isolated nucleic acid of claim 1, wherein said nucleotide sequence encodes a human Tcl-1b protein having an amino acid sequence of SEQ ID NO:39 from amino acid number 1 to 128.

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3. An isolated nucleic acid of not more than 50 kilobases which contains at least an 18 nucleotide portion encoding a Tcl-1b protein fragment.

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4. An isolated nucleic acid of not more than 50 kilobases which contains at least an 18 nucleotide portion of the sequence depicted in SEQ ID NO: 40.

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5. The isolated nucleic acid of claim 1, comprising a nucleotide sequence of SEQ ID NO:38 from nucleotide number 1 to 1152.

6. A Tcl-1b protein.

7. The isolated Tcl-1b protein of claim 6, comprising an amino acid sequence of SEQ. ID. NO: 39 from amino acid 1-128.

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8. An isolated nucleic acid, comprising a sequence encoding a fragment of a protein having an amino sequence of SEQ ID NO:39 from amino acid number 1 to 128, which fragment can be specifically bound by an antibody to a Tcl-1b protein.

9. A recombinant DNA vector, comprising a nucleotide sequence that encodes a Tcl-1b protein, wherein said nucleotide sequence is a cDNA sequence.

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10. A host cell that contains said recombinant DNA vector of claim 7.

11. The recombinant DNA vector of claim 7, wherein the nucleotide sequence encodes a human Tcl-1b protein having an amino acid sequence of SEQ ID NO:39 from amino acid number 1 to 128.

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12. An isolated nucleic acid of not more than 50 kilobases which contains at least a 50 nucleotide portion of SEQ ID NO: 40.

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13. An isolated nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to the cDNA sequence of SEQ ID NO:38, said nucleic acid containing at least an 25 nucleotide portion of SEQ ID NO:38.

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14. An isolated nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to a cDNA sequence that encodes a Tcl-1b protein, which protein has an amino acid sequence of SEQ ID NO:39, and said nucleic acid containing at least an 25 nucleotide portion of SEQ ID NO:38.

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15. An antisense molecule, comprising a nucleotide sequence complementary to at least a part of a coding sequence of a Tcl-1b protein, which is hybridizable to a Tcl-1b mRNA.

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16. The antisense molecule of claim 15, wherein said nucleotide sequence is complementary to at least a part of the sequence depicted in SEQ. ID. NO: 38.

5 17. A fusion protein comprising a Tcl-1b protein sequence of at least 10 amino acids linked to a non-Tcl-1b protein sequence.

18. An antibody which binds to an epitope of a Tcl-1b protien.

10 19. An isolated protein comprising an amino acid sequence having at least 70% amino acid sequence identity to an amino acid sequence depicted in SEQ. ID. NO: 39, over a contiguous sequence of at least 25 amino acids.

15 20. A method for detecting a target sequence indicative of a chromosome 14 abnormality in a sample, comprising the steps of:

- 20 a) amplifying said target sequence in said sample using a first primer of 18 to 25 nucleotides complementary to a TCL-1b nucleotide sequence of SEQ. ID. NO: 38, and a sencond primer complementary to a region telomeric or centromeric, preferably from a T-cell receptor α/δ locus, to said Tcl-1b gene; and
- 25 b) detecting any resulting amplified target sequence in which the presence of said amplified target sequence is indicative of said chromosome 14 abnormality.

21. The method of claim 20, wherein said chromosome 14 abnormality is in a Tcl-1b locus and comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

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22 A host cell that contains a recombinant vector comprising a cDNA sequence that encodes a human Tcl-1b protein having the amino acid sequence of SEQ ID NO:39 from amino acid number 1 to 128.

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23. A host cell that contains a recombinant vector comprising a nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to a cDNA sequence that encodes a Tcl-1b protein, which protein has the amino acid sequence of SEQ ID NO:39, and said nucleic acid containing at least an 25 nucleotide portion of SEQ ID NO:38.

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RI.126 24.
25. A pharmaceutical composition, comprising said antisense molecule of claim 15 or 16 in a pharmaceutically acceptable carrier.

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RI.126 25.
26. A pharmaceutical composition, comprising said antibody of claim 18 in a pharmaceutically acceptable carrier.

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RI.126 26.
27. A method for detecting a target nucleotide sequence indicative of a chromosome 14 abnormality in a nucleic acid sample, comprising the steps of:

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- a) hybridizing said sample with a nucleic acid probe of not more than 10 kilobases, comprising in the range of 15-1152 nucleotides complementary to said nucleotide sequence of SEQ. ID. NO: 38; and
- b) detecting or measuring an amount of any resulting hybridization between said probe and said target sequence within said sample.

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28. The method of claim 27, wherein said chromosome 14 abnormality is in a Tcl-1b locus and comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

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~~29.~~ A method for detecting a Tcl-1b protein in a patient sample, preferably a human sample, comprising:

- a) contacting said patient sample with an anti-Tcl-1b antibody under conditions such that immunospecific binding occurs; and
- b) detecting or measuring an amount of any immunospecific binding by said antibody.

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~~30.~~ A diagnostic kit, comprising in one or more containers, a pair of primers, each having at least 15-25 nucleotides, in which at least one of said primers is hybridizable to SEQ. ID. NO: 38 or its complement and wherein said primers are capable of priming DNA synthesis in a nucleic acid amplification reaction.

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~~31.~~ A method for treating a disease state associated with a chromosome 14 abnormality in a mammal, preferably a human, suffering from said disease state associated with said chromosome 14 abnormality, comprising administering a therapeutically effective amount of a Tcl-1b antisense molecule or an anti-Tcl-1b antibody to said mammal.

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~~31.~~

~~32.~~ The method of claim 31, wherein said disease state comprises a T-cell leukemia or lymphoma and said chromosome 14 abnormality comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

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~~32.~~

~~33.~~ An isolated nucleic acid comprising a nucleotide sequence encoding a Tng1 protein, wherein said nucleotide sequence is a cDNA sequence.

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~~34~~. The isolated nucleic acid of claim 33, wherein said nucleotide sequence encodes a human Tng1 protein having an amino acid sequence of SEQ ID NO:42 from amino acid number 1 to 141

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~~35~~. An isolated nucleic acid of not more than 50 kilobases which contains at least an 18 nucleotide portion encoding a Tng1 protein fragment.

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~~36~~. An isolated nucleic acid of not more than 50 kilobases which contains at least an 18 nucleotide portion of the sequence depicted in SEQ ID NO: 45.

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~~37~~. The isolated nucleic acid of claim 33, comprising a nucleotide sequence of SEQ ID NO:41 from nucleotide number 1 to 1500.

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~~38~~. A Tng1 protein.

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~~39~~. The isolated Tng1 protein of claim 38, comprising an amino acid sequence of SEQ. ID. NO: 42 from amino acid 1-141.

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~~40~~. An isolated nucleic acid, comprising a sequence encoding a fragment of a protein having an amino sequence of SEQ ID NO:42 from amino acid number 1 to 141, which fragment can be specifically bound by an antibody to a Tng1 protein.

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~~41~~. A recombinant DNA vector, comprising a nucleotide sequence that encodes a Tng1 protein, wherein said nucleotide sequence is a cDNA sequence.

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~~42~~. A host cell that contains said recombinant DNA vector of claim 39.

42. The recombinant DNA vector of claim 39, wherein the nucleotide sequence encodes a human Tng1 protein having an amino acid sequence of SEQ ID NO:42 from amino acid number 1 to 141.
- 5 R1.126 43. An isolated nucleic acid of not more than 50 kilobases which contains at least a 50 nucleotide portion of SEQ ID NO:45.
- 10 R1.126 44. An isolated nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to the cDNA sequence of SEQ ID NO:41, said nucleic acid containing at least an 25 nucleotide portion of SEQ ID NO:41.
- 15 R1.126 45. An isolated nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to a cDNA sequence that encodes a Tng1 protein, which protein has an amino acid sequence of SEQ. ID. NO: 42, and said nucleic acid containing at least an 25 nucleotide portion of SEQ. ID. NO: 41.
- 20 R1.126 46. An antisense molecule, comprising a nucleotide sequence complementary to at least a part of a coding sequence of a Tng1 protein, which is hybridizable to a Tng1 mRNA.
- 25 R1.126 47. The antisense molecule of claim 47, wherein said nucleotide sequence is complementary to a least a part of the sequence depicted in SEQ. ID. NO:41.
- 30 R1.126 48. A fusion protein comprising a Tng1 protein sequence of at least 10 amino acids linked to a non- Tng1 protein sequence.
- R1.126 49. An antibody which binds to an epitope of a Tng1 protien.

R1.126 ~~51~~⁵². An isolated protein comprising an amino acid sequence having at least 70% amino acid sequence identity to an amino acid sequence depicted in SEQ. ID. NO: 42, over a contiguous sequence of at least 25 amino acids.

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R1.126 ~~51~~⁵². A method for detecting a target sequence indicative of a chromosome 14 abnormality in a sample, comprising the steps of:

- 10 a) amplifying said target sequence in said sample using a first primer of 18 to 25 nucleotides complementary to a TNG1 nucleotide sequence of SEQ. ID. NO: 41, and a second primer complementary to a region telomeric or centromeric, preferably from a T-cell receptor α/δ locus, to said Tng1 gene; and
- 15 b) detecting any resulting amplified target sequence in which the presence of said amplified target sequence is indicative of said chromosome 14 abnormality.

R1.126 ~~52~~⁵³. The method of claim 52, wherein said chromosome 14 abnormality is in a Tng1 locus and comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

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R1.126 ~~53~~⁵⁴. A host cell that contains a recombinant vector comprising a cDNA sequence that encodes a human Tng1 protein having the amino acid sequence of SEQ. ID. NO: 42 from amino acid number 1 to 141.

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R1.126 ~~54~~⁵⁵. A host cell that contains a recombinant vector comprising a nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to a cDNA sequence that encodes a Tng1 protein, which protein has the amino acid sequence of SEQ. ID. NO: 42, and said nucleic acid containing at least an 25 nucleotide portion of SEQ. ID. NO: 41.

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56. A pharmaceutical composition, comprising said antisense molecule of claim 47 or 48 in a pharmaceutically acceptable carrier.

RI.126 56.
57. A pharmaceutical composition, comprising said antibody of claim 50 in a pharmaceutically acceptable carrier.

RI.126 57.
58. A method for detecting a target nucleotide sequence indicative of a chromosome 14 abnormality in a nucleic acid sample, comprising the steps of:

- 10 a) hybridizing said sample with a nucleic acid probe of not more than 10 kilobases, comprising in the range of 15-1500 nucleotides complementary to said nucleotide sequence of SEQ. ID. NO: 41; and
- 15 b) detecting or measuring an amount of any resulting hybridization between said probe and said target sequence within said sample.

RI.126 58.
59. The method of claim 58, wherein said chromosome 14 abnormality is in a Tng1 locus and comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

RI.126 59.
60. A method for detecting a Tng1 protein in a patient sample, preferably a human sample, comprising:

- 25 a) contacting said patient sample with an anti- Tng1 antibody under conditions such that immunospecific binding occurs; and
- b) detecting or measuring an amount of any immunospecific binding by said antibody.

RI.126 60.
61. A diagnostic kit, comprising in one or more containers, a pair of primers, each having at least 15-25 nucleotides, in which at least one of said primers is hybridizable to SEQ. ID. NO: 41 or it complement

and wherein said primers are capable of priming DNA synthesis in a nucleic acid amplification reaction.

5 ^{P1.126 61.}~~62.~~ A method for treating a disease state associated with a chromosome 14 abnormality in a mammal, preferably a human, suffering from said disease state associated with said chromosome 14 abnormality, comprising administering a therapeutically effective amount of a Tng1 antisense molecule or an anti- Tng1 antibody to said mammal.

10 ^{P1.126 62.}~~63.~~ The method of claim 62, wherein said disease state comprises a T-cell leukemia or lymphoma and said chromosome 14 abnormality comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

15 ^{P1.126 63.}~~64.~~ An isolated nucleic acid comprising a nucleotide sequence encoding a Tng2 protein, wherein said nucleotide sequence is a cDNA sequence.

20 ^{P1.126 64.}~~65.~~ The isolated nucleic acid of claim 64, wherein said nucleotide sequence encodes a human Tng2 protein having an amino acid sequence of SEQ. ID. NO: 44 from amino acid number 1 to 110.

25 ^{P1.126 65.}~~66.~~ An isolated nucleic acid of not more than 50 kilobases which contains at least an 18 nucleotide portion encoding a Tng2 protein fragment.

30 ^{P1.126 66.}~~67.~~ An isolated nucleic acid of not more than 50 kilobases which contains at least an 18 nucleotide portion of the sequence depicted in SEQ. ID. NO: 46.

R1.126 ~~67~~
~~68~~. The isolated nucleic acid of claim 64, comprising a nucleotide sequence of SEQ ID NO: 43 from nucleotide number 1 to XXX.

R1.126 ~~68~~
~~69~~. A Tng2 protein.

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R1.126 ~~69~~
~~70~~. The isolated Tng2 protein of claim 69, comprising an amino acid sequence of SEQ. ID. NO: 44 from amino acid 1-110.

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R1.126 ~~70~~
~~71~~. An isolated nucleic acid, comprising a sequence encoding a fragment of a protein having an amino sequence of SEQ. ID. NO:44 from amino acid number 1 to 110, which fragment can be specifically bound by an antibody to a Tng2 protein.

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~~72~~. A recombinant DNA vector, comprising a nucleotide sequence that encodes a Tng2 protein, wherein said nucleotide sequence is a cDNA sequence.

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~~73~~. A host cell that contains said recombinant DNA vector of claim 70.

R1.126 ~~73~~
~~74~~. The recombinant DNA vector of claim 70, wherein the nucleotide sequence encodes a human Tng2 protein having an amino acid sequence of SEQ ID NO:44 from amino acid number 1 to 110.

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~~75~~. An isolated nucleic acid of not more than 50 kilobases which contains at least a 50 nucleotide portion of SEQ ID NO:46.

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~~76~~. An isolated nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to the cDNA sequence of SEQ ID NO:43, said nucleic acid containing at least an 25 nucleotide portion of SEQ ID NO:43.

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An isolated nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to a cDNA sequence that encodes a Tng2 protein, which protein has an amino acid sequence of SEQ ID NO: 44, and said nucleic acid containing at least an 25 nucleotide portion of SEQ ID NO:43.

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An antisense molecule, comprising a nucleotide sequence complementary to at least a part of a coding sequence of a Tng2 protein, which is hybridizable to a Tng2 mRNA.

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The antisense molecule of claim 78, wherein said nucleotide sequence is complementary to a least a part of the sequence depicted in SEQ. ID. NO: 43.

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A fusion protein comprising a Tng2 protein sequence of at least 10 amino acids linked to a non- Tng2 protein sequence.

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An antibody which binds to an epitope of a Tng2 protien.

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An isolated protein comprising an amino acid sequence having at least 70% amino acid sequence identity to an amino acid sequence depicted in SEQ. ID. NO: 44, over a contiguous sequence of at least 25 amino acids.

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A method for detecting a target sequence indicative of a chromosome 14 abnormality in a sample, comprising the steps of:

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- a) amplifying said target sequence in said sample using a first primer of 18 to 25 nucleotides complementary to a TNG2nucleotide sequence of SEQ. ID. NO: 43, and a sencond primer complementary to a region telomeric or centromeric, preferably from a T-cell receptor α/δ locus, to said Tng2 gene; and

- b) detecting any resulting amplified target sequence in which the presence of said amplified target sequence is indicative of said chromosome 14 abnormality.

5 ^{83.}
P1.126 ~~84.~~ The method of claim 83, wherein said chromosome 14 abnormality is in a Tng2 locus and comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

10 ^{84.}
P1.126 ~~85.~~ A host cell that contains a recombinant vector comprising a cDNA sequence that encodes a human Tng2 protein having the amino acid sequence of SEQ ID NO: 44 from amino acid number 1 to 110.

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P1.126 ~~86.~~ A host cell that contains a recombinant vector comprising a nucleic acid that is capable of hybridizing under stringent conditions to a nucleotide sequence that is complementary to a cDNA sequence that encodes a Tng2 protein, which protein has the amino acid sequence of SEQ ID NO: 44, and said nucleic acid containing at least an 25 nucleotide portion of SEQ ID NO: 43.

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P1.126 ~~87.~~ A pharmaceutical composition, comprising said antisense molecule of claim 78 or 79 in a pharmaceutically acceptable carrier.

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P1.126 ~~88.~~ A pharmaceutical composition, comprising said antibody of claim 80 in a pharmaceutically acceptable carrier.

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P1.126 ~~89.~~ A method for detecting a target nucleotide sequence indicative of a chromosome 14 abnormality in a nucleic acid sample, comprising the steps of:

- a) hybridizing said sample with a nucleic acid probe of not more than 10 kilobases, comprising in the range of 15-2000 nucleotides complementary to said nucleotide sequence of SEQ. ID. NO: 43; and

b) detecting or measuring an amount of any resulting hybridization between said probe and said target sequence within said sample.

5 ^{21.126} ~~89~~ ~~90~~. The method of claim 89, wherein said chromosome 14 abnormality is in a Tng2 locus and comprises a t(14:14)(q11:q32) translocation or an inv (14)(q11:q32) inversion.

10 ^{21.126} ~~90~~ ~~91~~. A method for detecting a Tng2 protein in a patient sample, preferably a human sample, comprising:

a contacting said patient sample with an anti- Tng2 antibody under conditions such that immunospecific binding occurs; and

15 c) detecting or measuring an amount of any immunospecific binding by said antibody.

20 ^{21.126} ~~91~~ ~~92~~. A diagnostic kit, comprising in one or more containers, a pair of primers, each having at least 15-25 nucleotides, in which at least one of said primers is hybridizable to SEQ. ID. NO: 43 or its complement and wherein said primers are capable of priming DNA synthesis in a nucleic acid amplification reaction.

25 ^{21.126} ~~92~~ ~~93~~. A method for treating a disease state associated with a chromosome 14 abnormality in a mammal, preferably a human, suffering from said disease state associated with said chromosome 14 abnormality, comprising administering a therapeutically effective amount of a Tng2 antisense molecule or an anti- Tng2 antibody to said mammal.

30 ^{21.126} ~~93~~ ~~94~~. The method of claim 93, wherein said disease state comprises a T-cell leukemia or lymphoma and said chromosome 14 abnormality

comprises a t(14:14)(q11;q32) translocation or an inv (14)(q11;q32) inversion.